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Craniofacial features in patients with deficient and excessive growth hormone

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Abstract: We studied the role of growth hormone (GH) in craniofacial growth by analyzing the craniofacial structures in patients with either deficient or excessive GH. The cephalogrammes of 21 patients with isolated or combined GH deficiency and of two patients with GH excess were compared with cephalogrammes of age and sex matched controls, and the patients with deficient GH also with height and sex matched controls. In cephalometric measurements, skeletal anatomy was followed as closely as possible. All patients had a Class I or an end-to-end dental occlusion. Head circumference was normal in all patients. Facial widths were significantly smaller in patients with deficient GH but at the level of +2 SDs in the two with GH excess when compared to Finnish norms. In patients with deficient GH, facial heights were significantly smaller than in age matched controls, but of the same order with height controls for anterior facial height. Posterior facial height was smaller even in this comparison. In patients with GH excess, facial heights were much larger and at the levels of +3 and +6 SD. Clivus was shorter in patients with deficient GH and longer (+1.9 and +3 SD) in the two with GH excess. All angulations of the sphenoidal plane deviated from those of the controls in the group with GH deficiency. The cranial base angle (CL-SPhen) was smaller than in controls while it was normal in patients with GH excess. We are inclined to interpret the craniofacial structure of those with deficient GH as being unique to the condition rather than merely negative allometry. We conclude that a unique craniofacial configuration develops when a child grows with deficient or excessive GH. The configurations are not outwardly conspicuous, and the patients have a relatively normal facial appearance. It appears that the cartilaginous growth sites at the cranial base and mandible respond to the deficient or excessive GH and this is, to some extent, true with sutural and appositional facial growth as well.

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Key words: growth disorder–growth hormone–cephalometric study–pituitary gigantism–growth retardation–lack of growth hormone

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Introduction

Childhood growth is mainly regulated by the secretion of growth hormone (GH), provided that the nutritional status and other factors maintaining homeostasis are normal (Albertsson-Wikland and Rosberg, 1988). Children who repeatedly fail to secrete adequate amounts of GH despite pharmacological stimuli are diagnosed as having a classical GH deficiency. GH hypersecretion is diagnosed when GH secretion is constant and not suppressed by, e.g., hyperglycemia.

GH deficiency during childhood leads to progressive growth failure. The body proportions remain normal for age, but the facial appearance is characterized as "rounded" and "immature" [Brasel et al., 1965]. Adults with GH excess also have typical facial features described well by the condition known as "acromegaly" [Marie, 1886]. GH hypersecretion is rare during childhood, and thus the effects of GH excess on growing children are not well described.

With lateral cephalogrammes, Spiegel and coworkers [1971] studied 25 patients with anterior pituitary insufficiency and showed severe growth retardation in linear facial measurements. The deviation from normal was largest in posterior facial

height. They also noted a small cranial base angle when measured as the angle formed by clivus and the optic plane. Sharf and Laron [1971] studied a large group of patients with isolated GH deficiency, panhypopituitarism, and Laron type dwarfism (deficient IGF) with postero-anterior roentgenogrammes. Patients in all these groups had a clearly different head width/condylar width ratio than the healthy controls. The patients had a somewhat large bi-parietal width and a clearly smaller bicondylar width. In the investigators' opinion, this is a result of deficient cranial base development, and explains the "immature facies." Poole and coworkers (1982) described craniofacial features of 10 patients with isolated GH deficiency. They concluded that the face is clearly less affected than height, with the possible exception of posterior cranial base. Correction for bone age eliminated a lot of craniofacial abnormality.

Arcal enlargement, soft tissue growth, thick calvarium, enlarged frontal sinuses and prominent mandible are the classical morphological features of adult acromegaly already described by Pierre Marie in 1886. The most characteristic feature in the condition commencing before the closure of the epiphyses is excessive height. Whether there are specific craniofacial features typical for gigantism is not known. Moreover, there seems to be no proper cephalometric evaluation of the acromegalic face either.

By studying the craniofacial configuration of children with GH hypo- and hypersecretion, we are trying to elucidate the role of GH in craniofacial growth.

Patients and methods

Growth hormone deficiency

Twenty one patients with classical GH deficiency from various parts of Finland (17 males and four females aged 5.8–16.7) were studied. They were all examined and treated at the Growth Clinic of Childrens Hospital, University of Helsinki between 1972 and 1975 by authors HLL and SP. The diagnosis of GH deficiency is described in detail in earlier reports [Myllärniemi et al., 1978; Lenko et al., 1982]. The patients were treated with human GH (HGH). The roentgenogrammes used in this study were taken before any GH therapy in five patients, but 15 had had GH for 6–18 months and one for 30 months. All patients were prepubertal.

Growth hormone excess

Two patients, both females with GH excess, were studied. One of them had normal growth at 2 years but was 128 cm (+5 SD) tall at 5 years. An enlarged sella was noted and irradiated. At 14 years, her height was 202 cm, and an eosinofilic adenoma of the hypophysis was surgically removed. After the operation, panhypopituitarism and diabetes insipidus developed and the patient is on substitution therapy. The cephalogramme now studied was taken at 36 years. The other patient grew normally to 7.5 years but was 177 cm (+5 SD) tall at 12 years. A choromophobe adenoma was surgically removed, and ACTH, TSH, and gonadotrophin deficiency developed, but GH secretion remained high. Bromocriptine therapy was started at 15 years, (height; 190 cm) and the cepalogramme described here was taken at 16 years.

Methods

Head circumference was measured with a measuring tape as a horizontal measurement through glabella and opisthocranion. Length and width of the head and width of the face were measured with anthropometric curved calipers, according to Haataja [1963], and compared to his Finnish norms.

Lateral cephalometric radiographs were taken at the Department of Radiology, Institute of Dentistry, University of Helsinki. One age- and sex-matched and one height- and sex-matched control were chosen for each patient (except height controls for the 190-cm and 202-cm tall females) from the pretreatment files of the Department of Oral Development and Orthodontics, Institute of Dentistry, University of Turku; patients with only minor malocclusions were accepted as controls. The cephalogrammes were measured and read to the nearest 0.5 mm and to the nearest degree and corrected for enlargement. All measurements were performed by the same author (AM). Points, linear and angular measurements are shown in Figure 1 and listed in Tables 1 and 2. The significances of the means of differences between matched pairs of controls and patients were analyzed with a t-test.

Results

Growth hormone deficiency

Patients with isolated and combined pituitary deficiencies were analyzed separately, but as no differences between the patient groups were detected, the findings were pooled. Head circumference did not differ from the age- and sex-specific Finnish norms. Width of the head (eyrion-eyrion dimension) was of the same order with the published normal values as well, but width of the face both at zygion and gonion was significantly smaller. Mean difference at zygion was 8.3 mm and 9.0 mm at gonion. Nine

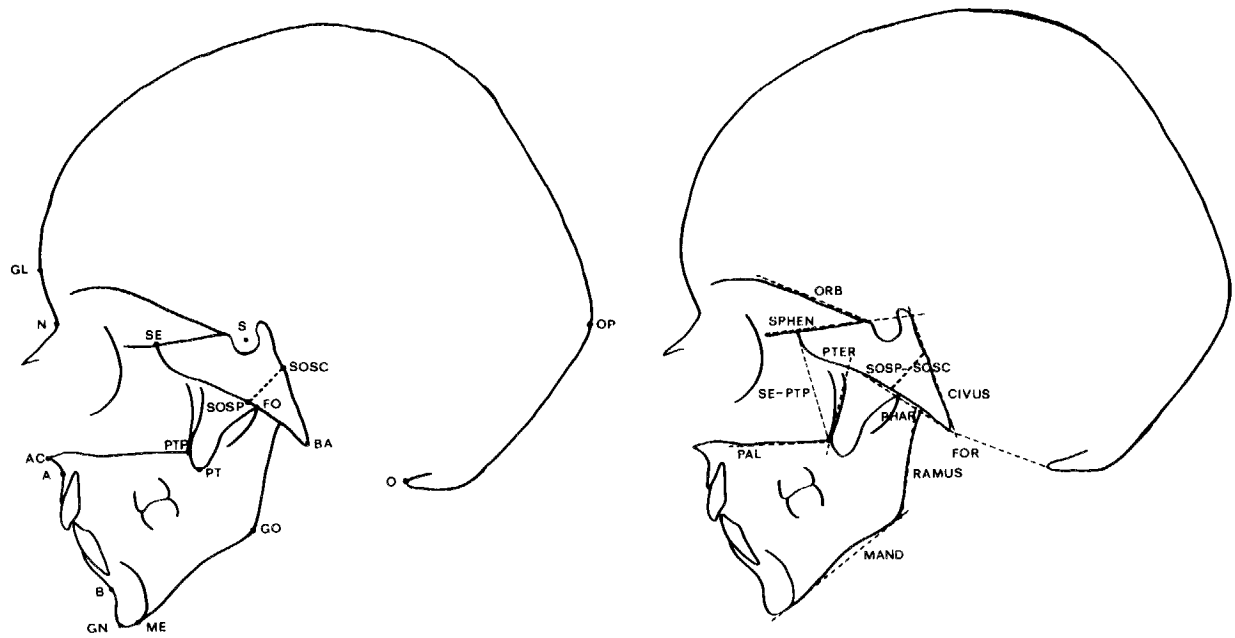

Fig. 1. The points and lines used in the analysis Points: **GL,** glabella; **Op** opisthhokranion; **N** nasion; **S** sella; **Ba** basion; **O** opisthion; **SE** the intersection of the great wing of the sphenoid and the sphenoethmoidal plane; **SOSC** the spheno-cranial end point of the spheno-occipital synchondrosis; **SOSP** the spheno-pharyngeal end point of the synchondrosis; **F0** representing foramen ovale, at the intersection of the cranial base and ventral surface of the pterygoid process. **FO**-point is used in this work instead of the condylion point because of the difficulties to trace the condylion area in the lateral X-ray cephalogrammes of the patients; **Ptp** pterygopalatinal point: the intersection of the extension of the palatal line and the ventral surface of the pterygoid process; **Pt** tip of the pterygoid process; **Go** gonion; **Ac** acanthion; **A point; B point; Gn**gnathion; and **Me** menton.

Lines (planes): **Ba-O,** basion-opisthion, foraminal line (**FOR**); **SE-Ptp,** PtP-vertical, corresponding to PM-vertical (Enlow 1969); **ORB,** tangent to the posterior slope of the orbital roof; **SPHEN,** tangent to the spheno-ethmoidal line; **CLIVUS,** tangent to the cerebral surface of the clivus, dorsum sellae excluded; **PAL,** tangent to the nasal floor posterior to the incisal canal; **MAND,** tangent to the mandibular base; **RAMUS,** tangent to the posterior border of the ramus, condular process excluded; **PTER,** tangent to the anterior surface of the pterygoid process; **PHAR,** tangent to the pharyngeal surface of the clivus; and **SOSC-SOSP,** spheno-occipital synchondrosis.

of the 21 patients demonstrated Class I dental occlusion. In nine, the occlusion was in an end-to-end relationship. Three patients with deciduous dentition were not classified.

Visual inspection of the cephalogrammes revealed a very small pituitary fossa in eight of the 21 patients; four had isolated GH deficiency and four had multiple deficiencies. In six patients the sella was considered large. Three of them had isolated GH deficiency.

The lower border of the posterior cranial fossa appeared to be below the level of the extended palatal plane in 13/21 cases, giving an impression of a "hanging" posterior cranial fossa and an upwards tilted foramen magnum (Fig. 2). The measurements did not, however, support this impression, yielding a barely significant difference between the patients and their height controls, but not age controls for the O-PAL dimension (Table 1).

The face appeared small compared to the calvarium. Facial and cranial size relations were analyzed by calculating a facial height/head length ratio. The ratio was of the same order in the patients and their height-matched controls, but distinctly different from the age-matched ones.

The cranial base

In norma lateralis, length of foramen magnum (Ba-O) was significantly smaller in patients when compared to age-matched controls, but of the same order with controls of the same height (Table 1). Practically all other linear cranial base dimensions were smaller than those of age-matched and also height-matched controls. Anterior cranial base, measured as S-N distance, was shorter, clivus (S-Ba), especially its occipital part (SS0-Ba), was shorter. However, height of spheno-occipital synchondrosis (SOSC-SOSP) was of the same order in patients and in children in both control groups.

The cranial base angle (SPHEN/CLIVUS) was smaller, as was the SPHEN/ORB angle, but the angle SPHEN/FOR was larger in the patients (Table 2). However, the angle formed by clivus plane and foramen plane (CLIVUS/FOR) was the same in the patients and controls.

Table 1. Differences in linear dimensions between matched pairs of controls and patients with growth hormone deficiency, means and standard deviations, in millimeters

	Age-matched comparison			Height-matched comparison		
Variable	x̄	SD	P	x̄	SD	P
Gl-Op	8.85	13.61	<0.02	12.53	9.82	<0.001
Ba-O	4.71	3.57	<0.001	1.06	3.07	<0.2
S-Ba	5.77	3.27	<0.001	2.41	2.29	<0.001
S-N	5.36	3.99	<0.001	4.06	4.28	<0.001
S-SSO	1.90	2.00	<0.001	1.11	1.83	<0.001
Ba-Ac	8.50	6.10	<0.001	6.63	7.37	<0.005
Ptp-Ac	4.79	4.22	<0.001	4.44	4.71	<0.005
N-Ac	6.08	2.91	<0.001	0.94	2.55	<0.2
N-Me	13.17	6.78	<0.001	2.57	5.68	<0.2
Gn-Go	11.89	7.68	<0.001	4.59	5.48	<0.005
S-Fo	3.43	2.82	<0.001	1.67	2.04	<0.01
S-Go	11.61	6.20	<0.001	4.77	4.58	<0.005
Fo-Go	8.32	4.88	<0.001	2.89	4.01	<0.02
Fo-Gn	12.71	6.37	<0.001	4.39	5.96	<0.02
O-PAL	2.14	10.83	<0.4	4.91	9.04	<0.05
SOSP-SPHEN	1.83	3.24	<0.25	−0.36	2.54	<0.7
Pt-SPHEN	7.75	4.41	<0.001	3.50	2.40	<0.001
SOSC-SE	2.28	5.13	<0.1	1.86	4.08	<0.2
SOSC-SOSP	0.85	2.62	<0.2	0.42	1.81	<0.4

Table 2. Differences in angular dimensions between matched pairs of controls and patients with growth hormone deficiency, means and standard deviations, in degrees

	Age-matched comparison			Height-matched comparison		
Variable	x̄	SD	P	x̄	SD	P
SNA	3.36	4.63	<0.005	2.56	3.75	<0.02
SNB	3.40	5.23	<0.02	1.84	4.10	<0.1
NSBa	−3.84	7.12	<0.02	−2.44	6.31	<0.2
SBaO	−5.37	8.71	<0.01	−4.66	7.14	<0.02
SPHEN/ORB	−3.64	6.35	<0.02	−3.57	3.95	<0.005
SPHEN/CLIVUS	5.29	9.78	<0.05	9.07	9.54	<0.005
SPHEN/FOR	4.82	8.18	<0.02	−7.63	7.80	<0.005
SPHEN/PAL	0.00	5.70	—	1.31	5.76	<0.4
SPHEN/MAND	−1.16	7.65	<0.6	1.94	8.04	<0.4
SPHEN/RAMUS	9.68	10.27	<0.001	8.56	13.60	<0.025
SPHEN/PTER	2.46	9.06	<0.3	2.25	7.05	<0.3
SPHEN/PHAR	2.26	7.65	<0.2	0.17	9.88	—
SPHEN/SOSC-SOSP	0.05	10.70	—	3.96	8.29	<0.1
SPHEN/SEVert	−4.52	8.69	<0.025	0.69	8.44	<0.8
ORB/CLIVUS	1.45	10.02	—	3.37	8.61	<0.2
ORB/FOR	1.39	6.56	—	7.94	8.81	<0.005
CLIVUS/FOR	−0.55	9.18	—	−2.23	10.41	<0.5
CLIVUS/PAL	7.45	11.56	<0.02	8.10	9.91	<0.01
CLIVUS/PHAR	−7.67	13.36	<0.5	−6.73	10.21	<0.025
CLIVUS/SEVert	8.79	14.03	<0.2	7.40	15.14	<0.1
FOR/PAL	−4.91	9.15	<0.2	−7.00	6.73	<0.001
PAL/MAND	0.58	7.97	—	0.84	8.29	—
PAL/RAMUS	8.90	9.24	<0.001	7.09	10.94	<0.025
PAL/SEvert	−2.96	13.64		3.00	10.77	—
MAND/RAMUS	−6.21	15.23	<0.1	0.91	12.01	—
SOCP-Ba-SOSC	−1.03	8.39	<0.6	−1.61	4.21	<0.2

Facial dimensions

Facial height (N-Me) was significantly smaller in the patients when compared to age-matched controls, but of the same order with children of the same height. Posterior facial height (S-Go) was, however, significantly smaller also when compared to controls of the same height. All linear dimensions related to the mandible were significantly smaller in patients with hypopituitarism than in controls of the same height (Table 1). Dimensions describing the

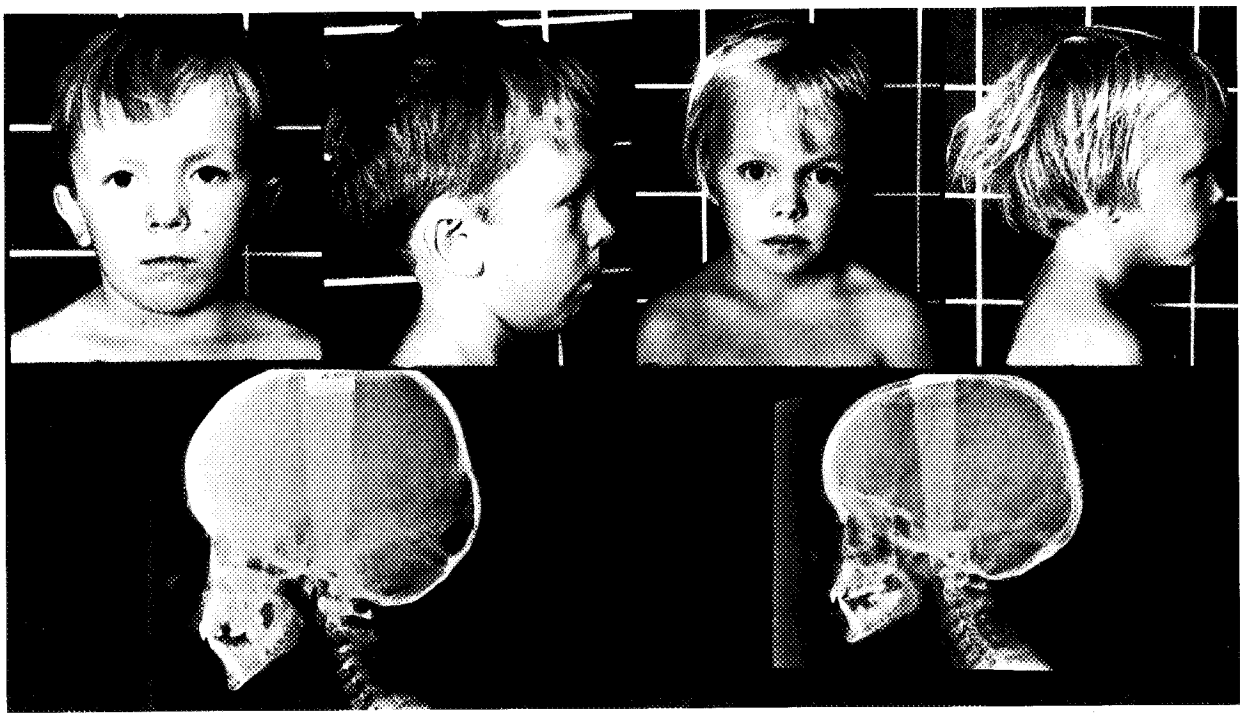

Fig. 2. Facial photographs and cephalogrammes of two boys with isolated GH deficiency aged 10.6, 113.5 cm on the left and 9.7, 118.0 cm on the right. "Immature" and "rounded" facial appearance, seen in both of the patients is typical of the condition.

depth of the face and the maxilla (Ba-Ac, Ptm-Ac) were significantly smaller than in controls, also in height-matched comparison. Even the angles SNA and SNB were smaller in the age-matched comparison.

Growth hormone excess

Both patients had relatively normal dental occlusion. Facial photographs and cephalogrammes of the two patients with GH excess are shown in Figure 3. Relatively normal facial appearance is obvious especially in the case of the older patient (patient 1), while the mandible in the younger one appears quite large. Thick calvarium and large frontal sinuses are evident in both patients. Head circumferences were 62 and 56 cm. Head length measurements showed normal values. Width dimensions of the head and the face were close to +2SD level in both of the patients. The angular cephalometric measurements were of the same order with the controls, except for the angle PAL/MAND, which showed values 27° and 33° compared to 16.5° and 23.3° in the controls. All linear dimensions were large when compared with the controls. The ones listed in Table 2 were very much larger than in the controls in both of the patients. Dimensions of the first and second cervical vertebrae were also larger than those in the controls.

Discussion

Our analysis of craniofacial features in patients with deficient GH demonstrated that a special craniofacial configuration developed, during years of poor growth due to deficient GH, before the condition was diagnosed and treatment instituted. We believe that a comparison with healthy children of the same height greatly helped in defining the areas in the craniofacial complex that are the most susceptible to deficient GH. We are inclined to interpret the craniofacial structures of those with deficient GH as being unique to the condition rather than merely negative allometry. The main craniofacial features of children with deficient GH are: normal size and shape of the calvarium, facial and calvarial size harmonious with height (but facial size small for age), anteriorly downward tilted sphenoidal plane, upwards tilted foramen plane, short posterior cranial base, small cranial base angle (SPHEN/CLIVUS), narrow and short face, small mandible, short maxilla and normal dental occlusion. We have earlier demonstrated delayed development of permanent teeth (+0.5 . . . –6 SD) in the same patients [Myllärniemi et al., 1978]. Our findings of small cranial base angle (SPHEN/CLIVUS) confirms that of Spiegel et al. (1971) as the sphenoidal plane is practically identical with the optic plane that was

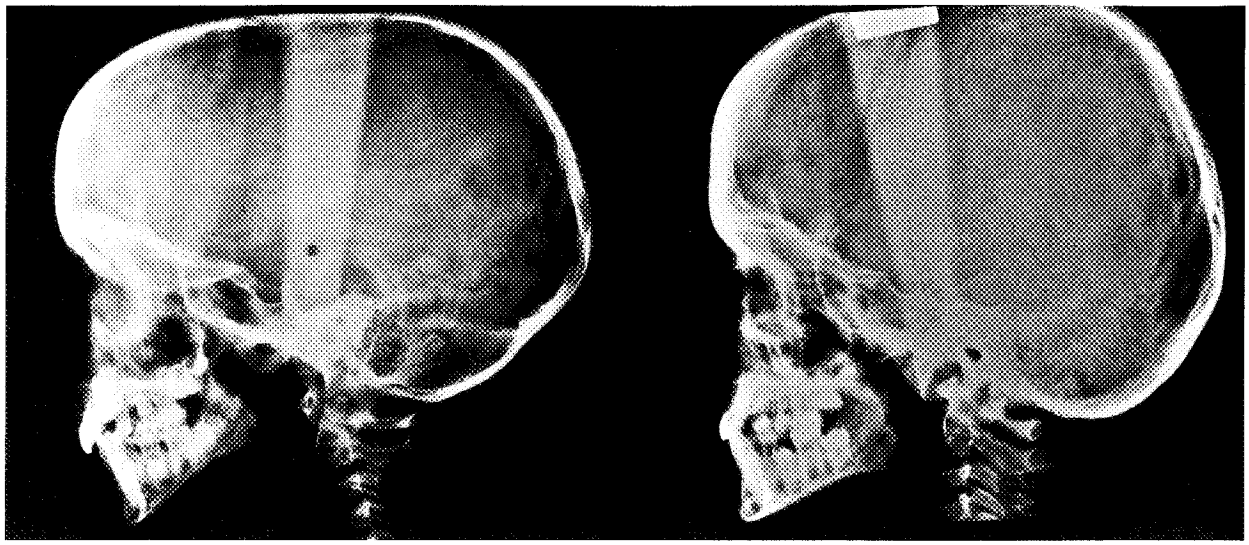

Fig. 3. Cephalogrammes of two patients with GH deficiency, aged 6.2 and 14.3. Note "hanging" posterior cranial fossa and tilted plane of foramen magnum.

used in their study. They also noted deficient posterior cranial base growth. The observed special inclination of the sphenoidal plane is difficult to explain. It might be an indication of altered head balance in these children, who are consistently smaller than their peers. In achodroplastic dwarfs, hyperextension of the head has been proposed by Cohen et al. [1985] as an explanation for the bony protuberances seen in these patients in the occipital bone, where the rectus capitis muscles attach.

Our cephalometric analysis of the two patients with GH excess is, to our knowledge, the first quantitative analysis of craniofacial changes in this rare condition (Table 3, Fig. 3). Excessive growth had taken place where growth was reduced in patients with deficient GH. Thus, considerable growth at clivus and considerable mandibular growth had taken place during the years the patients had been secreting excessive amounts of GH. Antero-posteriorly, the maxillary dimensions had remained relatively normal, but the maxilla had translocated anteriorly and forward leaving a wide posterior nasal space (Pt-Sphen). Maxilla had more or less followed the mandible and normal dental relations had been maintained. In acromegaly, the adult form of GH excess, mandibular prognatism and crossbite of anterior teeth often develops, but mostly so slowly that the patient or his family do not notice the change [Pelkonen, 1984]. Normal mandibular growth is believed to continue very slowly in the third and fourth decades of life. Increased adrenal androgenic function has been demonstrated in acromegalia [Mautalen and Mellinger, 1965], which could also play a role in excessive mandibular growth typical of acromegaly. Martucci et al. [1989] analyzed the face of 11 patients with the condition, but it is obvious that one cannot describe the grossly aberrant facial features seen in acromegaly by means of conventional cephalometry.

Width dimensions of the face differed characteristically from the Finnish age-specific standards in the two groups of patients. They were small in those with deficient GH and large in the two with GH excess. This can partly reflect changes in the width of the cranial base, but could also reflect the influence of tongue growth, possibly also differences in respiratory capacity and nasal volume. Findings related to increased facial width dimensions in these patients are supported by the experimental results in rodents of Savostin-Asling et al. [1980].

In cephalometric studies the choice of dimensions from the multitude of radiographic shadows is naturally of decisive importance. In the present analysis skeletal anatomy has been followed as well as possible, while also employing some time-honored landmarks to facilitate comparisons with some earlier data in the literature. A basic problem in cephalometrics and craniometrics is a workable reference system. In recent literature, the so-called reference-free system of analysis has been advocated [Moss et al., 1985; Bookstein, 1987]. In the present work, we have used the more conventional way of measuring craniofacial dimensions, but most of the measurements do not depend on any line of reference. In phylogenetic and comparative anatomical studies, the clivus has been claimed to be the most conservative part of the skull base and thus

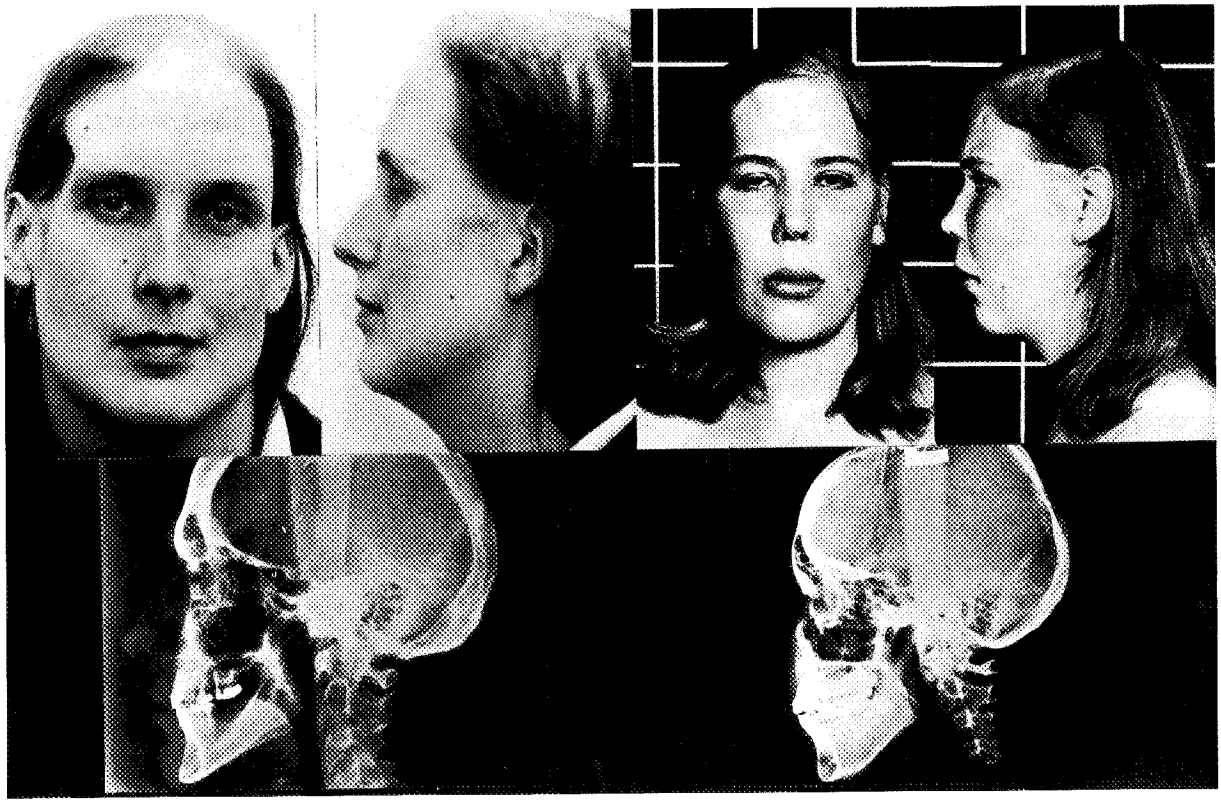

Fig. 4. Facial photographs and cephalogrammes of two female patients with pituitary gigantism. Patient 1 on the left, 36, 203 cm, and patient 2 on the right, 16.3, 190 cm. Note considerable width of the face especially in patient 1. Patient 2 clearly has developed sc acromegaloid features, while they are absent in patient 1.

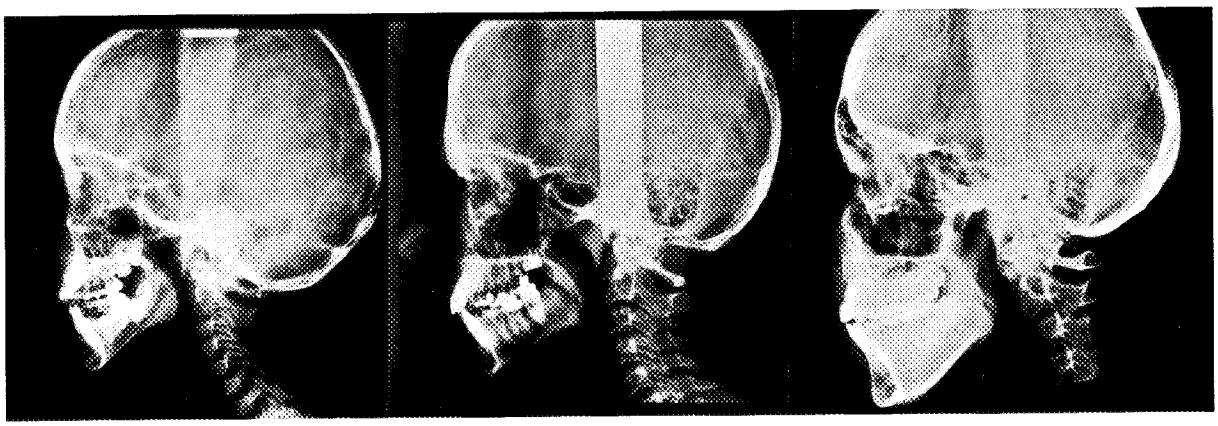

Fig. 5. Lateral cephalogrammes of the 16.7-year-old boy (122 cm) with untreated hypopituitarism on the left, of a healthy 16.7-year-old boy (174 cm) in the middle and of the 16.3-year-old girl (190 cm) with excessive growth hormone secretion on the right set side by side by comparison.

recommendable for the line of reference [Dabelow, 1929; Hofer, 1954; Moss, 1958; Koski, 1961]. Ontogenetically, the surface of the clivus has been seen to be subjected to remodelling [Melsen, 1974]; nevertheless, radiographically its relationship to other parts of the skull base have been found to be very closely similar in healthy children and adults [Vinkka and Koski, 1975]. Thus, directional changes within the craniofacial skeleton found in the patients with deficient GH have been related to the clivus in the present analysis. It can also be pointed out that there are no "silent" tissue areas in

Table 3. Differences (mm) in seven craniofacial dimensions between two female patients aged 36 (pat 1) and 16 (pat 2) with pituitary gigantism and their controls[a]

Measured dimension	Difference between patient and control			
	patient 1		patient 2	
	mm	SDS	mm	SDS
Length of clivus (S-BA)	10.5	+3.0	6.6	+1.9
Length of corpus mandibulae (Gn-Go)	7.1	+2.0	7.2	+2.0
Height of ramus mandibulae (Fo-Go)**	14.1	+4.1	14.4	+4.2
Depth of the face (Ba-Ac)	13.6	+2.0	6.6	+0.9
Anterior facial height (N-Me)	31.0	+6.8	23.0	+3.3
Posterior facial height (S-Go)	14.1	+3.7	19.0	+4.9
Posterior nasal area height (Pt-Sphen)	10.3	*	9.0	*

*SD not known

**SD for AR-Go

[a] In an attempt to quantify the observed deviations they are expressed in standard deviation units (SDS) using available or most suitable age- and sex-specific population SD:s given by Koski (1960) and Riolo et al. (1974), corrected for enlargement.

the cranium, and it can be assumed that if the observed differences are to the same direction in both age- and stature-matched comparisons, possible remodelling effects do not have to be counted.

Growth of the occipital part of the clivus takes place both at the spheno-occipital synchondrosis and at the anterior border of foramen magnum [Melsen, 1974]. Measured from radiocephalogrammes, this part grows considerably more than the sphenoid part of the clivus, especially during the prepubertal period [Latham, 1972; Nakamura et al., 1972]. The differences between the patients with lack of GH and their matched controls seem to reflect this normal growth gradient. The similarity between the patients and their age- and stature-matched controls, regarding the angle between the clivus and foramen magnum lines, is not surprising as the occipital part of the clivus and the foramen belong to the same occipital bone, and have been found to move as a unit even in cases of artificial deformations of the skull [Moss, 1958]. The region of the attachment of the skull to the vertebral column and of the brain stem apparently is a basic, relatively stable part within a species.

A small pituitary fossa was noted in the cephalogrammes of eight patients with hypopituitarism, while a large sella was seen in six of these patients. Considerable variation is usually seen in the size of the pituitary fossa in cephalogrammes taken for orthodontic purposes. In the last few years, computed tomography (CT) has revealed a picture of an empty sella in some children with hypopituitarism. At present, magnetic resonance imaging (MRI) is considered superior to CT in studying hypothalamic and pituitary anatomic conditions [Radfar et al., 1985]. In a study with MRI of 30 patients with hypopituitarism, the smallest pituitary volume was observed in children with multiple endocrine defects [Pellini, 1990]. Enlarged sella occurs in children with juveline hypothyroidism [Andersen, 1960].

GH has no specific target organ. Virtually every tissue system responds to the action of GH, which primarily is an anabolic hormone. However, GH has profound effects on cartilage growth, which is mediated by insulin-like growth factor I (IGF-I). A hypothetical model for the stimulatory effect of GH on longitudinal bone growth is given by Isaksson et al. [1987]. IGF-I and IGF-II have been shown also to increase bone collagen synthesis and decrease collagen degradation in cultures of calvaria [McCarthy et al. 1989]. Craniofacial growth changes with deficient or excessive GH were most conspicious in the clivus and mandible; the cartilaginous spheno-occipital synchondrosis and the condylar cartilage clearly responded to deficient or excessive GH. An effect of GH was also seen in sutural and appositional facial growth.

From our study of 21 young patients with deficient GH and two rare cases of GH excess, we conclude that a specific craniofacial configuration develops while the patient grows. The configurations are not very conspicious. The patients have a relatively normal facial appearance, although the face is narrow in deficient GH and broad in GH excess. Head circumference and length are not affected, but facial and cranial base dimensions and their mutual relations are. It appears that the cartilaginous growth sites at the cranial base and in the mandible respond to deficient or excessive GH. Sutural and appositional facial growth mechanisms are also affected.

Our patients with deficient GH were treated with human GH (HGH) and the effect of this treatment

on facial growth will soon be reported. Recombinant GH (rGH) in big doses is now utilized in various conditions of growth failure. The effect of these treatments on facial as well as statural growth should be monitored.

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